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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,852	09/22/2000	Per Johan Lundberg	1103326-0686	1116

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PATENT DEPARTMENT
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EXAMINER	
TRAN, SUSAN T	
ART UNIT	**PAPER NUMBER**
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/646,852	LUNDBERG ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12-18,20 and 23-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,12-18,20 and 23-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

Claims 1, 3, 6-8, 12-18, 20 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. US 5,753,265.

Nara teaches a controlled release composition comprising a drug-containing core coated with a protective coating layer containing hydrophilic substances (column 6, lines 1-10). Hydrophilic substances include hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methylcellulose, polyvinylpyrrolidone, and polyvinyl alcohol (column 5, lines 1-4). The amount of this protective coating is about 1 to about 15% to the core (ID). Drugs include omeprazole and lansoprazole (column 3, lines 59-60). The drug is mixed with excipient, such as sucrose or calcium phosphate (osmotic agent); binder; disintegrant, such as, sodium crosslinked carboxymethylcellulose or low-substitutional hydroxypropyl cellulose (swelling agent); and lubricant, including talc (alkaline additive) (column 5, lines 36-52; and examples). The core can be in the form of a granule, fine granule, or inert carrier particles including sucrose (column 5, lines 30-35, and 60-65). The coated core can be prepared in tablet or capsule form for oral administration (column 6, lines 56-65; and claim 7).

Nara does not explicitly teach the addition of a modifying agent in the protective coating composition.

Bergstrand teaches an omeprazole core is coated with a separating layer (protective coating layer) comprising polymer such as ethylcellulose, hydroxypropyl

methylcellulose, polyvinylpyrrolidone, methylcellulose, and polyvinyl alcohol (column 7, lines 51-61). Bergstrand further teaches the polymer can be used alone (as a single polymer) (column 7, line 62). The separating layer further comprises plasticizer, and antistatic agents such as talc (column 7, lines 63-65; and examples 1, 3 and 7). Thus, it would have been obvious to one of ordinary skill in the art to modify the protective coating composition of Nara to include additives such as talc in view of the teaching of Bergstrand to obtain the claimed invention, because Bergstrand teaches adding talc to the coating composition to increase the thickness of the layer and thereby strengthen the diffusion barrier, because Bergstrand teaches the separating layer improves the chemical stability of the active substance and the physical properties of the dosage form (column 8, lines 21-27), because Nara teaches the desirability of using a separating layer to protect the acid sensitive active core, and because Nara teaches the use of other agent to help modify the coating properties (modifying agent) (example 11, lines 49-50).

Regarding the limitation "water-insoluble polymer capable of forming a semipermeable membrane", it is noted that Nara and Bergstrand teach the use of the claimed water-insoluble polymers. Therefore, the burden is shifted to applicant to show that the water-insoluble polymers taught by Nara and Bergstrand do not have the claimed property. This is because identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. US 5,753,265 and Hodges et al. US 5,225,202.

Nara is relied upon for the reason stated above. Nara does not explicitly teach the amount of alkaline additive present in the core.

Hodges teaches a controlled release pellet comprising acid labile drug in the core, and one or more buffering agents (alkaline additives) (see abstract, and column 3, lines 1-4; lines 15-19). Buffering agents present in the core in an amount ranging from about 1 to about 20% (column 3, lines 34-36). Thus, it would have been obvious to one of ordinary skill in the art to use alkaline additive in an amount taught by Hodges to obtain a stable acid labile composition, because Hodges teaches using buffering agent in an amount of about 1 to about 20% to aid in minimizing drug degradation in the core due to acid ingress in low pH environments (column 3, lines 6-9), and because Nara teaches a composition with low toxicity and can be safely used in mammals.

It is noted that Nara does not explicitly teach the weight ratio of the modifying agent to water-insoluble substance, as well as the amount of the alkaline additive and swelling agent in the core. However, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Thus, it would have been obvious to one of ordinary skill in the

art to, by routine experimentation determine suitable amount of talc in the core composition as well as in the coating composition, because Nara teaches the release rate of the active ingredient is mainly in the small and large intestine without an enteric coating, while the release rate of the active ingredient is very limited in the stomach (column 1, lines 53-55; and column 7, lines 25-31), and because Nara teaches a coated formulation with low toxicity that can be safely used in human. The expected result would be a controlled-release composition comprising omeprazole in the core without enteric coating that can limit release of omeprazole in the stomach, but increases release in the small and large intestine.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. and, Zentner US 4,795,644 or Lundberg et al. 6,013,281.

Nara is relied upon for the reasons stated above. Nara is silent of the claimed alkaline agent.

Zentner teaches pH-modifying agent includes sodium mono- or di-phosphate (column 8, lines 3-15).

Lundberg teaches alkaline reacting compound includes arginine (column 6, lines 50-55). Thus, it would have been obvious to one of ordinary skill in the art to modify the compositions of Nara using sodium mono- or di-phosphate and arginine compound as an alkaline agent, because the references teach suitable composition for the same

active agent, namely, omeprazole, and because Nara teaches the desirability of using an alkaline agent in the composition.

Claims 4, 5 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al., and Cotton et al. WO 98/54171.

Nara is relied upon for the reasons stated above. Nara is deficient in the fact that Nara does not specifically teach magnesium salt of omeprazole.

Cotton teaches novel form of S-enantiomer of omeprazole, including S-omeprazole, and more specifically, magnesium salt of S-omeprazole trihydrate (hereafter, the compound) (see abstract, and page 1, lines 4-10). Cotton also teaches the compound is formulated into oral dosage form, *e.g.*, capsule, tablet, and the like (page 6, lines 15-30). The formulation is effective as a gastric acid secretion inhibitor and is useful as an anti-ulcer agent (page 6, lines 1-14).

Cotton does not explicitly teaches the compound having a crystallinity of more than 70%, however, Cotton teaches that the compound of his invention is highly crystalline, *i.e.*, having a higher crystallinity than any other form of magnesium salt of S-omeprazole in the prior art (page 3, lines 24 through page 4, lines 1-7). Therefore, the burden is shifted to applicant to show the compound taught by Cotton does not have the crystallinity being claimed. It is also noted that Cotton teaches the trihydrate form, *e.g.*, magnesium salt of S-omeprazole "trihydrate". However, applicant claims recite a generic form of magnesium salt of S-omeprazole with the transitional phrase

"comprising of" permits any other form, including "trihydrate" taught by Cotton. Thus, it would have been obvious for one of ordinary skill in the art to modify the controlled release composition comprising a drug-containing core coated with a *non-enteric* coating composition using the magnesium salt of S-omeprazole trihydrate in view of the teaching of Cotton, because Cotton teaches the compound of his invention is more stable, easier to handle and store, easier to synthesize in a reproducible manner, because Cotton teaches the compound is most preferred in oral administration formulation, because Nara teaches a non-enteric coated formulation with low toxicity that can be safely used in human. The expected result would be a controlled-release composition comprising omeprazole in the core without enteric coating that can limit release of omeprazole in the stomach, but increases release in the small and large intestine.

Response to Arguments

Applicant's arguments filed 09/21/07 have been fully considered but they are not persuasive.

Applicant argues that in contrast to the claimed invention, Nara discloses a coating composition comprised of two or three polymers: a water insoluble polymer; a swellable polymer; and an optional hydrophilic substance (See claims 1 and 9). Such a two- or there-polymer system does not suggest the single polymer coating composition of the claimed invention. In summary, Nara discloses a coating composition comprising at least two polymers: a water insoluble polymer and a swellable polymer. Thus, it can

be said that Nara teaches away from the claimed invention which is characterized by a semipermeable membrane comprising a single polymer composition containing a water insoluble polymer.

However, in response to applicant's arguments, it is noted that the comprising language in the preamble of the claims does not preclude the separating/protective coating layer taught by Nara, as long as it is a coating layer comprising a single polymer. Nara clearly teaches a coating layer comprising a single polymer such as ethyl cellulose (column 6, lines 4-10; and example 11). Accordingly, Nara meets the requirement for the limitation coating comprises a single polymer.

Applicant argues that the combination of Nara and Bergstrand fails to suggest the claimed invention since the coating composition disclosed by the primary reference to Nara is characterized by a mixture of two or three polymers: a water insoluble polymer; a swellable polymer; and an optional hydrophilic substance. In contrast, the claimed dosage form is distinguishable over the cited combination of references by a semipermeable membrane comprising a single polymer composition containing a water insoluble polymer and wherein the dosage form is not enteric coated.

However, as discussed above, the Nara reference clearly teaches a coating layer that comprises a single polymer such as ethyl cellulose. Thus, the combination of Nara and Bergstrand suggests the claimed invention.

Applicant argues that the combinations of Nara and Bergstrand and Hodges, or Nara and Bergstrand and Zentner or Lundberg, or Nara and Bergstrand and Cotton fail to suggests the claimed invention since the coating composition disclosed by the

primary reference to Nara is characterized by a mixture of two or three polymers: a water insoluble polymer; a swellable polymer; and an optional hydrophilic substance.

However, as stated above, the Nara reference clearly teaches a coating layer that comprises a single polymer such as ethyl cellulose. Accordingly, the teaching of Nara meets the claimed limitations.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN TRAN
PRIMARY EXAMINER

Art Unit 1615